

**WE CLAIM:**

5 1. A method of increasing the battery life of an alternating current iontophoretic device used to transport a compound of interest through a localized region of a patient's body tissue, comprising:

(a) applying an alternating current to a localized region of body tissue having an inherent barrier limiting the transport of compounds therethrough, the alternating current generated using an alternating current iontophoretic device and applied at a level  
10 sufficient both to decrease the electrical resistance of the body tissue to a target resistance level and to maintain the electrical resistance of the body tissue at said target level; and

(b) either prior to, during, or both prior to and during application of the alternating current, delivering to the localized region of body tissue an amount of at least one barrier-modifying agent effective to alter the penetration barrier so as to reduce the voltage level  
15 necessary to achieve and maintain said target resistance level thereby facilitating transport of a compound of interest across the body tissue.

20 2. The method of claim 1, wherein the barrier-modifying agent is delivered to the localized region of body tissue prior to step (a).

3. The method of claim 1, wherein the barrier-modifying agent is delivered to the localized region of body tissue during step (a).

25 4. The method of claim 1, wherein the barrier-modifying agent is delivered to the localized region of body tissue both prior to and during step (a).

5. The method of claim 1, wherein the barrier-modifying agent is selected from the group consisting of fatty acids, fatty alcohols, bile acids, bile salts, nonionic surfactants, anionic surfactants, cationic surfactants, amphoteric surfactants, hydrocarbon

solvents, esters, amides, pyrrolidones, sulfoxides, cyclodextrins, N-alkyl-azacycloalkanones, N-alkyl-azacycloalkenones, urea, alkyl-substituted urea, dialkyl-substituted urea, aryl-substituted urea, diaryl-substituted urea, terpenes, and combinations thereof.

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6. The method of claim 5, wherein the barrier-modifying agent is selected from the group consisting of fatty acids, fatty alcohols, bile acids, nonionic surfactants, anionic surfactants, pyrrolidones, and combinations thereof.

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7. The method of claim 6, wherein the barrier-modifying agent is a fatty acid.

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8. The method of claim 7, wherein the fatty acid is selected from the group consisting of arachidic acid, arachidonic acid, behenic acid, capric acid, caproic acid (n-hexanoic acid), caproleic acid, caprilic acid, docosadienoic acid, docosaheptaenoic acid, docosapentaenoic acid, eicosadienoic acid, eicosahexaenoic acid, eicosapentaenoic acid, eicosatrienoic acid, elaidic acid (*trans*-9-octadecanoic acid), eleosteric acid, erucic acid, heneicosanoic acid, heptacosanoic acid, heptadecanoic acid, heptanoic acid, hexacosanoic acid, isostearic acid, lauric acid, lignoceric acid, linoleic acid, linoelaidic acid,  $\alpha$ -linolenic acid,  $\gamma$ -linolenic acid, myristic acid, myristoleic acid, neodecanoic acid, nervonic acid, nonacosanoic acid, nonadecanoic acid, octacosanoic acid, oleic acid, palmitic acid (n-hexadecanoic acid), palmitoleic acid, pelargonic acid, pentadecanoic acid, pentacosanoic acid, petroselenic acid, phytanic acid, stearic acid, triacontanoic acid, tricosanoic acid, tridecanoic acid, and undecanoic acid, vaccenic acid, and combinations thereof.

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9. The method of claim 8, wherein the fatty acid is selected from the group consisting of capric acid, lauric acid, oleic acid, and combinations thereof.

10. The method of claim 6, wherein the barrier-modifying agent is a fatty alcohol.

11. The method of claim 10, wherein the fatty alcohol is selected from the group consisting of behenyl alcohol, cetyl alcohol, elaidyl alcohol, erucyl alcohol, isostearyl alcohol, lauryl alcohol, myristyl alcohol, oleyl alcohol, palmitoleyl alcohol, petroselinyl alcohol, stearyl alcohol, and combinations thereof.

12. The method of claim 6, wherein the barrier-modifying agent is a bile acid or bile salt.

13. The method of claim 12, wherein the barrier-modifying agent is selected from the group consisting of cholic acid, deoxycholic acid, lithocholic acid, chenodeoxycholic acid, and ursodeoxycholic acid, taurocholic acid, taurodeoxycholic acid, tauroolithocholic acid, taurochenodeoxycholic acid, tauroursodeoxycholic acid, glycocholic acid, glycodeoxycholic acid, glycolithocholic acid, glycochenodeoxycholic acid, glyoursodeoxycholic acid, sodium cholate, sodium taurocholate, sodium glycocholate, sodium deoxycholate, sodium taurodeoxycholate, sodium glycodeoxycholate, sodium ursodeoxycholate, sodium chenodeoxycholate, sodium taurochenodeoxycholate, sodium taurochenodeoxycholate, sodium N-methyl taurocholate, and combinations thereof.

14. The method of claim 6, wherein the barrier-modifying agent is a nonionic surfactant.

15. The method of claim 14, wherein the nonionic surfactant is selected from the group consisting of: esters of fatty acids; C<sub>6</sub>-C<sub>22</sub> alkyl esters of monohydric alcohols, diols and polyols; C<sub>6</sub>-C<sub>22</sub> alkenyl esters of monohydric alcohols, diols and polyols; diols esterified with a fatty acid and with a polyoxyalkylene; polyols esterified with a fatty acid and with a polyoxyalkylene; polyoxyalkylene fatty acid esters; polyoxyalkylene fatty ethers; polyglyceryl fatty acid esters; and combinations thereof.

16. The method of claim 15, wherein the nonionic surfactant is selected from the group consisting of cetyl lactate, myristyl lactate, lauryl lactate, isostearyl lactate, and stearyl lactate, ethyl lactate, isopropyl myristate, isopropyl palmitate, ethyl linoleate, isopropyl linoleate, methyl laurate, ethyl oleate, isopropyl n-decanoate, isopropyl  
5 myristate, isopropyl palmitate, sucrose monooleate, cholesterol stearate, octyldodecyl myristate, propylene glycol dilaurate, propylene glycol monooleate, propylene glycol dioctanoate, propylene glycol dicaprylate, propylene glycol dicaprinate, glycerol monolaurate, glycerol monooleate, glycerol monostearate; the sorbitan fatty acid esters sorbitan monopalmitate, sorbitan monooleate, sorbitan dioleate, sorbitan trioleate,  
10 sorbitan sesquioleate, sorbitan isostearate, sorbitan diisostearate, sorbitan tristearate, and sorbitan monolaurate; and the sucrose fatty acid esters sucrose monooleate, sucrose monostearate, sucrose monolaurate, sucrose distearate, sucrose dipalmitate, sucrose monopalmitate, polyoxyethylene glyceryl fatty acid esters, polyoxypropylene glyceryl fatty acid esters, polyoxyethylene sorbitan fatty acid esters, polyoxypropylene sorbitan  
15 fatty acid esters, diethyleneglycol lauryl ether, polyoxyethylene fatty ethers, polyglyceryl fatty acid esters, and combinations thereof.

17. The method of claim 6, wherein the barrier-modifying agent is an anionic surfactant.

18. The method of claim 17, wherein the anionic surfactant is selected from the group consisting of sodium n-dodecyl sulfate, dialkyl sodium sulfosuccinates, sodium lauryl sulfate, sodium 7-ethyl-2-methyl-4-dodecyl sulfate, lithium n-dodecyl sulfate, sodium dodecylbenzene sulfonate, sodium oleate, sodium caprate, sodium laurate,  
25 sodium lauryl sarcosinate, sodium dioctyl sulfosuccinate, sodium caproate, sodium caprylate, sodium myristate, sodium myristolate, sodium palmitate, sodium palmitoleate, sodium ricinoleate, sodium linoleate, sodium linolenate, sodium stearate, sodium tetradecyl sulfate, sodium lauryl sarcosinate, sodium docusate, and combinations thereof.

19. The method of claim 6, wherein the barrier-modifying agent is a pyrrolidone.

20. The method of claim 19, wherein the pyrrolidone is selected from the group consisting of 2-pyrrolidone, N-methyl-2-pyrrolidone, 5-methyl-2-pyrrolidone, N-ethyl-2-pyrrolidone, 1,5-dimethyl-2-pyrrolidone, N-hexyl-2-pyrrolidone, N-benzyl-2-pyrrolidone, N-phenyl-2-pyrrolidone, N-lauryl-2-pyrrolidone, 4-carboxy-N-methyl-2-pyrrolidone, 4-carboxy-N-hexyl-2-pyrrolidone, 4-carboxy-N-lauryl-2-pyrrolidone, 4-methoxycarbonyl-N-methyl-2-pyrrolidone, 4-methoxycarbonyl-N-hexyl-2-pyrrolidone, 4-methoxycarbonyl-N-lauryl-2-pyrrolidone, 2-pyrrolidone-5-carboxylic acid and the decyl, oleyl and dodecyl esters thereof, N-farnesyl-2-pyrrolidone, 3-hydroxy-N-methyl-2-pyrrolidone, methylthioethyl pyrrolidone, 1-[2-(decylthio)ethyl]azacyclopentan-2-one, 2-mercaptoethylpyrrolidone, 1-dodecyl-2-pyrrolidone, 3-dodecyl-2-pyrrolidone, and combinations thereof.

21. The method of claim 1, wherein the barrier-modifying agent is effective to reduce the voltage required to achieve and maintain said target electrical resistance is at least 20% less than the voltage required to achieve and maintain said target electrical resistance in the absence of the barrier-modifying agent.

22. The method of claim 21, wherein the barrier-modifying agent is effective to reduce the voltage required to achieve and maintain said target electrical resistance is at least 50% less than the voltage required to achieve and maintain said target electrical resistance in the absence of the barrier-modifying agent.

23. The method of claim 22, wherein the barrier-modifying agent is effective to reduce the voltage required to achieve and maintain said target electrical resistance is at least 70% less than the voltage required to achieve and maintain said target electrical resistance in the absence of the barrier-modifying agent.

24. The method of claim 1, wherein the body tissue is skin.

25. The method of claim 1, wherein the body tissue is mucosal tissue.

5           26. The method of claim 1, wherein the alternating current is applied at a voltage level in the range of about 1 V to 75 V.

27. The method of claim 26, wherein the voltage level is in the range of about 1 V to 45 V.

10           28. The method of claim 27, wherein the voltage level is in the range of about 1 V to about 10 V.

15           29. The method of claim 28, wherein the direct current applied is in the range of about 0.1 to 10 V and about 0.01 to 0.5 mA/cm<sup>2</sup>.

30. The method of claim 1, further comprising applying direct current to the localized region of body surface.

20           31. The method of claim 30, wherein the direct current is applied as a prepulse prior to step (a).

32. The method of claim 31, wherein the direct current is superimposed over the alternating current during step (a).

25           33. The method of claim 31, wherein the direct current is applied both as a prepulse and is superimposed over the alternating current.

34. The method of claim 1, wherein the localized region of body tissue has an area in the range of approximately  $1\text{cm}^2$  to approximately  $100\text{ cm}^2$ .

5 35. The method of claim 34, wherein the localized region of body tissue has an area in the range of approximately  $5\text{ cm}^2$  to approximately  $30\text{ cm}^2$ .

36. The method of claim 1, wherein the compound of interest is an analyte extracted from within the patient's body, such that analyte is transported from beneath the localized region of the body surface to the exterior of the body.

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37. The method of claim 36, wherein the analyte is glucose.

38. The method of claim 36, wherein the analyte is an amino acid.

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39. The method of claim 36, wherein the amino acid is phenylalanine.

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40. The method of claim 36, wherein the analyte is selected from the group consisting of a marker of a disease state, a substance of abuse, an electrolyte, a mineral, a hormone, a peptide, a metal ion, a nucleotidic material, a gene, an enzyme, and metabolites thereof.

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41. The method of claim 36, wherein the analyte is selected from the group consisting of a monosaccharide, a disaccharide, an oligosaccharide, an organic acid, an alcohol, a fatty acid, cholesterol, an amino acid, zinc, iron, copper, magnesium, potassium, and metabolites thereof.

42. The method of claim 36, wherein the analyte is a pharmacologically active agent that has been administered to the patient.

43. The method of claim 42, wherein the analyte is selected from the group consisting of analeptic agents, analgesic agents, anesthetic agents, antiasthmatic agents, antiarthritic agents, anticancer agents, anticholinergic agents, anticonvulsant agents, antidepressant agents, antidiabetic agents, antidiarrheal agents, antiemetic agents, 5 antihelminthic agents, antihistamines, antihyperlipidemic agents, antihypertensive agents, anti-infective agents, antiinflammatory agents, antimigraine agents, antiparkinsonism agents, antipruritic agents, antipsychotic agents, antipyretic agents, antispasmodic agents, antitubercular agents, antiulcer agents, antiviral agents, anxiolytic agents, appetite suppressants, attention deficit disorder and attention deficit hyperactivity disorder drugs, 10 cardiovascular agents, central nervous system stimulants, diuretics, genetic materials, hormonolytics, hypnotics, hypoglycemic agents, immunosuppressive agents, muscle relaxants, narcotic antagonists, nicotine, nutritional agents, parasympatholytics, peptide drugs, psychostimulants, sedatives, steroids, smoking cessation agents, sympathomimetics, tranquilizers, vasodilators,  $\beta$ -agonists, tocolytic agents, and 15 metabolites thereof.

44. The method of claim 36, wherein at least two analytes are extracted concurrently.

20 45. The method of claim 1, wherein the alternating current is applied to the localized region of the body tissue for a time period in the range of approximately 10 minutes to greater than 24 hours.

46. The method of claim 45, wherein the time period is in the range of 25 approximately 10 minutes to approximately 12 hours.

47. The method of claim 45, wherein the time period is in the range of approximately 12 hours to approximately 24 hours.



48. The method of claim 1, wherein the barrier-modifying agent reduces the amount of time required to achieve said target electrical resistance.

49. The method of claim 48, wherein the barrier-modifying agent reduces the amount of time required to achieve said target electrical resistance by at least 20%.

50. The method of claim 49, wherein the barrier-modifying agent reduces the amount of time required to achieve said target electrical resistance by at least 50%.

51. The method of claim 50, wherein the barrier-modifying agent reduces the amount of time required to achieve said target electrical resistance by at least 70%.

52. An alternating current iontophoresis device for extracting an analyte from a patient's body beneath a localized region of body tissue, comprising:

- a) a first electrode assembly adapted to receive an analyte and be placed in ion-conducting and analyte-receiving relation with respect to the localized region of body tissue, the assembly comprising a reservoir for collecting and containing an analyte extracted from the patient's body beneath the localized region;
- b) a second electrode assembly adapted to be placed in ion-transmitting relation with the body tissue at a location spaced apart from the first electrode assembly; and
- c) an alternating current source electrically connected to the first and second electrode assemblies, for applying an alternating current to the localized region of body tissue at a level sufficient to achieve and maintain a target electrical resistance within the tissue,

wherein at least one of the first and second electrode assemblies further comprises a barrier-modifying agent for delivery to the localized region of the body tissue, said

agent effective to reduce the voltage required to achieve and maintain said target electrical resistance.

53. The device of claim 52, further comprising a direct current source electrically  
5 connected to the first and second electrode assemblies.

54. The device of claim 52, wherein the barrier-modifying agent is selected from  
the group consisting of fatty acids, fatty alcohols, bile acids, bile salts, nonionic  
surfactants, anionic surfactants, cationic surfactants, amphoteric surfactants, hydrocarbon  
10 solvents, esters, amides, pyrrolidones, sulfoxides, cyclodextrins, N-alkyl-  
azacycloalkanones, N-alkyl-azacycloalkenones, urea, alkyl-substituted urea, dialkyl-  
substituted urea, aryl-substituted urea, diaryl-substituted urea, terpenes, and combinations  
thereof.

55. The device of claim 54, wherein the barrier-modifying agent is selected from  
15 the group consisting of fatty acids, fatty alcohols, bile acids, nonionic surfactants, anionic  
surfactants, pyrrolidones, and combinations thereof.

56. The device of claim 52, wherein the second electrode assembly further  
20 comprises a secondary reservoir for collecting and containing one or more analytes  
extracted from the body tissue at the second electrode.

57. An alternating current iontophoresis device for delivering a  
pharmacologically active agent to a patient through a localized region of the patient's  
25 body surface, comprising:

- a) a first electrode assembly adapted to be placed in ion-conducting and  
compound-delivering relation with the localized region of the body  
surface and comprising a reservoir housing a pharmacologically active  
agent to be transported into and through the body surface; and

- b) a second electrode assembly adapted to be placed in ion-transmitting relation with the body surface at a location spaced apart from the first electrode assembly; and
- c) an alternating current source electrically connected to the first and second electrode assemblies, for applying an alternating current to the localized region of body tissue at a level sufficient to achieve and maintain a target electrical resistance within the localized region,

wherein at least one of the first and second electrode assemblies further comprises a barrier-modifying agent for delivery to the localized region of the body tissue, said agent effective to reduce the voltage necessary to achieve and maintain a target electrical resistance within the localized region.

58. The device of claim 57, further comprising a direct current source electrically connected to the first and second electrode assemblies.

59. The device of claim 57, wherein the barrier-modifying agent is selected from the group consisting of fatty acids, fatty alcohols, bile acids, bile salts, nonionic surfactants, anionic surfactants, cationic surfactants, amphoteric surfactants, hydrocarbon solvents, esters, amides, pyrrolidones, sulfoxides, cyclodextrins, N-alkyl-azacycloalkanones, N-alkyl-azacycloalkenones, urea, alkyl-substituted urea, dialkyl-substituted urea, aryl-substituted urea, diaryl-substituted urea, terpenes, and combinations thereof.

60. The device of claim 59, wherein the barrier-modifying agent is selected from the group consisting of fatty acids, fatty alcohols, bile acids, nonionic surfactants, anionic surfactants, pyrrolidones, and combinations thereof.

61. The device of claim 57, wherein the second electrode assembly further comprises a secondary reservoir housing a pharmacologically active agent to be transported through the body surface at the second electrode.